

RAW SEQUENCE LISTING

**The Biotechnology Systems Branch of the Scientific and Technical
Information Center (STIC) no errors detected.**

Application Serial Number: 10/527,411
Source: PT/10
Date Processed by STIC: 3/25/05

ENTERED



PCT

RAW SEQUENCE LISTING

DATE: 03/25/2005

PATENT APPLICATION: US/10/527,411

TIME: 11:00:40

Input Set : A:\sequence listing ascii.txt

Output Set: N:\CRF4\03252005\J527411.raw

```

3 <110> APPLICANT: Shone, Clifford
4     Foster, Keith Alan
5     Chaddock, John
6     Marks, Philip
7     Sutton, J. Mark
8     Stancombe, Patrick
9     Wayne, Jonathan
11 <120> TITLE OF INVENTION: Recombinant Toxin Fragments
13 <130> FILE REFERENCE: 1581.0130005
C--> 15 <140> CURRENT APPLICATION NUMBER: US/10/527,411
C--> 15 <141> CURRENT FILING DATE: 2005-03-11
15 <150> PRIOR APPLICATION NUMBER: PCT/GB2003/003824
16 <151> PRIOR FILING DATE: 2003-09-12
18 <150> PRIOR APPLICATION NUMBER: US 10/241,596
19 <151> PRIOR FILING DATE: 2002-09-12
22 <160> NUMBER OF SEQ ID NOS: 175
24 <170> SOFTWARE: PatentIn version 3.2
26 <210> SEQ ID NO: 1
27 <211> LENGTH: 2616
28 <212> TYPE: DNA
29 <213> ORGANISM: Clostridium botulinum
32 <220> FEATURE:
33 <221> NAME/KEY: CDS
34 <222> LOCATION: (1)..(2616)
36 <400> SEQUENCE: 1
37 atg cag ttc gtg aac aag cag ttc aac tat aag gac cct gta aac ggt      48
38 Met Gln Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
39 1          5          10          15
41 gtt gac att gcc tac atc aaa att cca aac gcc ggc cag atg cag ccg      96
42 Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
43          20          25          30
45 gtg aag gct ttc aag att cat aac aaa atc tgg gtt att ccg gaa cgc      144
46 Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
47          35          40          45
49 gat aca ttt acg aac ccg gaa gaa gga gac ttg aac ccg ccg ccg gaa      192
50 Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
51          50          55          60
53 gca aag cag gtg cca gtt tca tac tac gat tca acc tat ctg agc aca      240
54 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
55 65          70          75          80
57 gac aac gag aag gat aac tac ctg aag gga gac acc aaa tta ttc gag      288
58 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
59          85          90          95

```

RAW SEQUENCE LISTING

DATE: 03/25/2005

PATENT APPLICATION: US/10/527,411

TIME: 11:00:40

Input Set : A:\sequence listing ascii.txt

Output Set: N:\CRF4\03252005\J527411.raw

61	cgt att tat tcc act gac ctg ggc cgt atg ctg ctg acc tca atc gtc	336
62	Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val	
63	100 105 110	
65	cgc gga atc cca ttt tgg ggt ggc agt acc att gac acg gag ttg aag	384
66	Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys	
67	115 120 125	
69	gtt att gac act aac tgc att aac gtg atc caa cca gac ggt agc tac	432
70	Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr	
71	130 135 140	
73	aga tct gaa gaa ctt aac ctc gta atc atc ggg ccc tcc gcg gac att	480
74	Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile	
75	145 150 155 160	
77	atc cag ttt gag tgc aag agc ttt ggc cac gaa gtg ttg aac ctg acg	528
78	Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr	
79	165 170 175	
81	cgt aac ggt tac ggc tct act cag tac att cgt ttc agc cca gac ttc	576
82	Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe	
83	180 185 190	
85	acg ttc ggt ttc gag gag agc ctg gag gtt gat acc aac ccg ctg ttg	624
86	Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu	
87	195 200 205	
89	ggt gca ggc aag ttc gca act gat cca gcg gtg acc ctg gca cac gag	672
90	Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu	
91	210 215 220	
93	ctg atc cac gcc ggt cat cgt ctg tat ggc att gcg att aac ccg aac	720
94	Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn	
95	225 230 235 240	
97	cgc gtg ttc aag gtt aac acc aac gcc tac tac gag atg agt ggt tta	768
98	Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu	
99	245 250 255	
101	gaa gta agc ttc gag gaa ctg cgc acg ttc ggt ggc cat gat gcg aag	816
102	Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys	
103	260 265 270	
105	ttt atc gac agc ttg cag gag aac gag ttc cgt ctg tac tac tac aac	864
106	Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn	
107	275 280 285	
109	aag ttt aaa gat att gca agt aca ctg aac aag gct aag tcc att gtg	912
110	Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val	
111	290 295 300	
113	ggt acc act gct tca tta cag tat atg aaa aat gtt ttt aaa gag aaa	960
114	Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys	
115	305 310 315 320	
117	tat ctc cta tct gaa gat aca tct gga aaa ttt tcg gta gat aaa tta	1008
118	Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu	
119	325 330 335	
121	aaa ttt gat aag tta tac aaa atg tta aca gag att tac aca gag gat	1056
122	Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp	
123	340 345 350	
125	aat ttt gtt aag ttt ttt aaa gta ctt aac aga aaa aca tat ttg aat	1104

RAW SEQUENCE LISTING

DATE: 03/25/2005

PATENT APPLICATION: US/10/527,411

TIME: 11:00:40

Input Set : A:\sequence listing ascii.txt

Output Set: N:\CRF4\03252005\J527411.raw

126	Asn	Phe	Val	Lys	Phe	Phe	Lys	Val	Leu	Asn	Arg	Lys	Thr	Tyr	Leu	Asn	
127			355					360					365				
129	ttt	gat	aaa	gcc	gta	ttt	aag	ata	aat	ata	gta	cct	aag	gta	aat	tac	1152
130	Phe	Asp	Lys	Ala	Val	Phe	Lys	Ile	Asn	Ile	Val	Pro	Lys	Val	Asn	Tyr	
131			370				375					380					
133	aca	ata	tat	gat	gga	ttt	aat	tta	aga	aat	aca	aat	tta	gca	gca	aac	1200
134	Thr	Ile	Tyr	Asp	Gly	Phe	Asn	Leu	Arg	Asn	Thr	Asn	Leu	Ala	Ala	Asn	
135	385					390					395					400	
137	ttt	aat	ggg	caa	aat	aca	gaa	att	aat	aat	atg	aat	ttt	act	aaa	cta	1248
138	Phe	Asn	Gly	Gln	Asn	Thr	Glu	Ile	Asn	Asn	Met	Asn	Phe	Thr	Lys	Leu	
139					405					410					415		
141	aaa	aat	ttt	act	gga	ttg	ttt	gaa	ttt	tat	aag	ttg	cta	tgt	gta	aga	1296
142	Lys	Asn	Phe	Thr	Gly	Leu	Phe	Glu	Phe	Tyr	Lys	Leu	Leu	Cys	Val	Arg	
143				420					425					430			
145	ggg	ata	ata	act	tct	aaa	act	aaa	tca	tta	gat	aaa	gga	tac	aat	aag	1344
146	Gly	Ile	Ile	Thr	Ser	Lys	Thr	Lys	Ser	Leu	Asp	Lys	Gly	Tyr	Asn	Lys	
147			435					440					445				
149	gca	tta	aat	gat	tta	tgt	atc	aaa	gtt	aat	aat	tgg	gac	ttg	ttt	ttt	1392
150	Ala	Leu	Asn	Asp	Leu	Cys	Ile	Lys	Val	Asn	Asn	Trp	Asp	Leu	Phe	Phe	
151		450				455					460						
153	agt	cct	tca	gaa	gat	aat	ttt	act	aat	gat	cta	aat	aaa	gga	gaa	gaa	1440
154	Ser	Pro	Ser	Glu	Asp	Asn	Phe	Thr	Asn	Asp	Leu	Asn	Lys	Gly	Glu	Glu	
155	465				470					475					480		
157	att	aca	tct	gat	act	aat	ata	gaa	gca	gca	gaa	gaa	aat	att	agt	tta	1488
158	Ile	Thr	Ser	Asp	Thr	Asn	Ile	Glu	Ala	Ala	Glu	Glu	Asn	Ile	Ser	Leu	
159				485					490						495		
161	gat	tta	ata	caa	caa	tat	tat	tta	acc	ttt	aat	ttt	gat	aat	gaa	cct	1536
162	Asp	Leu	Ile	Gln	Gln	Tyr	Tyr	Leu	Thr	Phe	Asn	Phe	Asp	Asn	Glu	Pro	
163			500						505				510				
165	gaa	aat	att	tca	ata	gaa	aat	ctt	tca	agt	gac	att	ata	ggc	caa	tta	1584
166	Glu	Asn	Ile	Ser	Ile	Glu	Asn	Leu	Ser	Ser	Asp	Ile	Ile	Gly	Gln	Leu	
167			515					520					525				
169	gaa	ctt	atg	cct	aat	ata	gaa	aga	ttt	cct	aat	gga	aaa	aag	tat	gag	1632
170	Glu	Leu	Met	Pro	Asn	Ile	Glu	Arg	Phe	Pro	Asn	Gly	Lys	Lys	Tyr	Glu	
171		530				535						540					
173	tta	gat	aaa	tat	act	atg	ttc	cat	tat	ctt	cgt	gct	caa	gaa	ttt	gaa	1680
174	Leu	Asp	Lys	Tyr	Thr	Met	Phe	His	Tyr	Leu	Arg	Ala	Gln	Glu	Phe	Glu	
175	545				550					555					560		
177	cat	ggg	aaa	tct	agg	att	gct	tta	aca	aat	tct	gtt	aac	gaa	gca	tta	1728
178	His	Gly	Lys	Ser	Arg	Ile	Ala	Leu	Thr	Asn	Ser	Val	Asn	Glu	Ala	Leu	
179				565					570					575			
181	tta	aat	cct	agt	cgt	gtt	tat	aca	ttt	ttt	tct	tca	gac	tat	gta	aag	1776
182	Leu	Asn	Pro	Ser	Arg	Val	Tyr	Thr	Phe	Phe	Ser	Ser	Asp	Tyr	Val	Lys	
183			580					585					590				
185	aaa	gtt	aat	aaa	gct	acg	gag	gca	gct	atg	ttt	tta	ggc	tgg	gta	gaa	1824
186	Lys	Val	Asn	Lys	Ala	Thr	Glu	Ala	Ala	Met	Phe	Leu	Gly	Trp	Val	Glu	
187			595				600					605					
189	caa	tta	gta	tat	gat	ttt	acc	gat	gaa	act	agc	gaa	gta	agt	act	acg	1872
190	Gln	Leu	Val	Tyr	Asp	Phe	Thr	Asp	Glu	Thr	Ser	Glu	Val	Ser	Thr	Thr	

RAW SEQUENCE LISTING

DATE: 03/25/2005

PATENT APPLICATION: US/10/527,411

TIME: 11:00:40

Input Set : A:\sequence listing ascii.txt

Output Set: N:\CRF4\03252005\J527411.raw

```

191      610      615      620
193 gat aaa att gcg gat ata act ata att att cca tat ata gga cct gct      1920
194 Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro Ala
195 625      630      635      640
197 tta aat ata ggt aat atg tta tat aaa gat gat ttt gta ggt gct tta      1968
198 Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu
199      645      650      655
201 ata ttt tca gga gct gtt att ctg tta gaa ttt ata cca gag att gca      2016
202 Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala
203      660      665      670
205 ata cct gta tta ggt act ttt gca ctt gta tca tat att gcg aat aag      2064
206 Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys
207      675      680      685
209 gtt cta acc gtt caa aca ata gat aat gct tta agt aaa aga aat gaa      2112
210 Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu
211      690      695      700
213 aaa tgg gat gag gtc tat aaa tat ata gta aca aat tgg tta gca aag      2160
214 Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys
215 705      710      715      720
217 gtt aat aca cag att gat cta ata aga aaa aaa atg aaa gaa gct tta      2208
218 Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu
219      725      730      735
221 gaa aat caa gca gaa gca aca aag gct ata ata aac tat cag tat aat      2256
222 Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn
223      740      745      750
225 caa tat act gag gaa gag aaa aat aat att aat ttt aat att gat gat      2304
226 Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp
227      755      760      765
229 tta agt tcg aaa ctt aat gag tct ata aat aaa gct atg att aat ata      2352
230 Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile
231      770      775      780
233 aat aaa ttt ttg aat caa tgc tct gtt tca tat tta atg aat tct atg      2400
234 Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met
235 785      790      795      800
237 atc cct tat ggt gtt aaa cgg tta gaa gat ttt gat gct agt ctt aaa      2448
238 Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys
239      805      810      815
241 gat gca tta tta aag tat ata tat gat aat aga gga act tta att ggt      2496
242 Asp Ala Leu Leu Lys Tyr Ile Tyr Asp Asn Arg Gly Thr Leu Ile Gly
243      820      825      830
245 caa gta gat aga tta aaa gat aaa gtt aat aat aca ctt agt aca gat      2544
246 Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp
247      835      840      845
249 ata cct ttt cag ctt tcc aaa tac gta gat aat caa aga tta tta tct      2592
250 Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser
251      850      855      860
253 aca ttt act gaa tat att aag taa      2616
254 Thr Phe Thr Glu Tyr Ile Lys
255 865      870

```

RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/527,411

DATE: 03/25/2005

TIME: 11:00:40

Input Set : A:\sequence listing ascii.txt

Output Set: N:\CRF4\03252005\J527411.raw

```

258 <210> SEQ ID NO: 2
259 <211> LENGTH: 871
260 <212> TYPE: PRT
261 <213> ORGANISM: Clostridium botulinum
263 <400> SEQUENCE: 2
265 Met Gln Phe Val Asn Lys Gln Phe Asn Tyr Lys Asp Pro Val Asn Gly
266 1 5 10 15
269 Val Asp Ile Ala Tyr Ile Lys Ile Pro Asn Ala Gly Gln Met Gln Pro
270 20 25 30
273 Val Lys Ala Phe Lys Ile His Asn Lys Ile Trp Val Ile Pro Glu Arg
274 35 40 45
277 Asp Thr Phe Thr Asn Pro Glu Glu Gly Asp Leu Asn Pro Pro Pro Glu
278 50 55 60
281 Ala Lys Gln Val Pro Val Ser Tyr Tyr Asp Ser Thr Tyr Leu Ser Thr
282 65 70 75 80
285 Asp Asn Glu Lys Asp Asn Tyr Leu Lys Gly Val Thr Lys Leu Phe Glu
286 85 90 95
289 Arg Ile Tyr Ser Thr Asp Leu Gly Arg Met Leu Leu Thr Ser Ile Val
290 100 105 110
293 Arg Gly Ile Pro Phe Trp Gly Gly Ser Thr Ile Asp Thr Glu Leu Lys
294 115 120 125
297 Val Ile Asp Thr Asn Cys Ile Asn Val Ile Gln Pro Asp Gly Ser Tyr
298 130 135 140
301 Arg Ser Glu Glu Leu Asn Leu Val Ile Ile Gly Pro Ser Ala Asp Ile
302 145 150 155 160
305 Ile Gln Phe Glu Cys Lys Ser Phe Gly His Glu Val Leu Asn Leu Thr
306 165 170 175
309 Arg Asn Gly Tyr Gly Ser Thr Gln Tyr Ile Arg Phe Ser Pro Asp Phe
310 180 185 190
313 Thr Phe Gly Phe Glu Glu Ser Leu Glu Val Asp Thr Asn Pro Leu Leu
314 195 200 205
317 Gly Ala Gly Lys Phe Ala Thr Asp Pro Ala Val Thr Leu Ala His Glu
318 210 215 220
321 Leu Ile His Ala Gly His Arg Leu Tyr Gly Ile Ala Ile Asn Pro Asn
322 225 230 235 240
325 Arg Val Phe Lys Val Asn Thr Asn Ala Tyr Tyr Glu Met Ser Gly Leu
326 245 250 255
329 Glu Val Ser Phe Glu Glu Leu Arg Thr Phe Gly Gly His Asp Ala Lys
330 260 265 270
333 Phe Ile Asp Ser Leu Gln Glu Asn Glu Phe Arg Leu Tyr Tyr Tyr Asn
334 275 280 285
337 Lys Phe Lys Asp Ile Ala Ser Thr Leu Asn Lys Ala Lys Ser Ile Val
338 290 295 300
341 Gly Thr Thr Ala Ser Leu Gln Tyr Met Lys Asn Val Phe Lys Glu Lys
342 305 310 315 320
345 Tyr Leu Leu Ser Glu Asp Thr Ser Gly Lys Phe Ser Val Asp Lys Leu
346 325 330 335
349 Lys Phe Asp Lys Leu Tyr Lys Met Leu Thr Glu Ile Tyr Thr Glu Asp
350 340 345 350

```

VERIFICATION SUMMARY

PATENT APPLICATION: US/10/527,411

DATE: 03/25/2005

TIME: 11:00:41

Input Set : A:\sequence listing ascii.txt

Output Set: N:\CRF4\03252005\J527411.raw

L:15 M:270 C: Current Application Number differs, Replaced Current Application No
L:15 M:271 C: Current Filing Date differs, Replaced Current Filing Date